

## SEQUENCE LISTING

<110> Keler, Tibor  
Deo, Yashwant

<120> HUMAN MONOCLONAL ANTIBODIES TO HER2/NEU

<130> MXI-160US

<140> US 10/031,722

<141> 2002-01-18

<150> PCT/US00/20272

<151> 2000-07-25

<150> US 60/146,313

<151> 1999-07-29

<150> US 60/188,539

<151> 2000-03-10

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<170> PatentIn Ver. 2.0

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<221> CDS

<222> (1) .. (372)

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| gag | gtg | cag | ctg | ttg | gag | tct | ggg | gga | ggc | ttg | gta | cag | cct | ggg | ggg | 48  |
| Glu | Val | Gln | Leu | Leu | Glu | Ser | Gly | Gly | Gly | Leu | Val | Gln | Pro | Gly | Gly |     |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |     |
| tcc | ctg | aga | ctc | tcc | tgt | gca | gcc | tct | gga | ttc | acc | ttt | agc | agc | tat | 96  |
| Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Thr | Phe | Ser | Ser | Tyr |     |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |     |
| gcc | atg | acc | tgg | gtc | cgc | cag | gct | cca | ggg | aag | ggg | ctg | gag | tgg | gtc | 144 |
| Ala | Met | Thr | Trp | Val | Arg | Gln | Ala | Pro | Gly | Lys | Gly | Leu | Glu | Trp | Val |     |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |
| tca | gct | atc | agt | ggt | agt | ggt | tat | agc | aca | tac | tac | gca | gac | tcc | gag | 192 |
| Ser | Ala | Ile | Ser | Gly | Ser | Gly | Tyr | Ser | Thr | Tyr | Tyr | Ala | Asp | Ser | Glu |     |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |     |
| aag | ggc | cgg | ttc | acc | atc | tcc | aga | gac | aat | tcc | aag | aac | acg | ctg | tat | 240 |
| Lys | Gly | Arg | Phe | Thr | Ile | Ser | Arg | Asp | Asn | Ser | Lys | Asn | Thr | Leu | Tyr |     |
| 65  |     |     |     |     | 70  |     |     |     | 75  |     |     |     |     | 80  |     |     |
| ctg | caa | atg | aac | agc | ctg | aga | gcc | gag | gac | acg | gcc | gta | tat | tac | tgt | 288 |
| Leu | Gln | Met | Asn | Ser | Leu | Arg | Ala | Glu | Asp | Thr | Ala | Val | Tyr | Tyr | Cys |     |
|     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |
| gcg | aaa | ggg | ttt | cag | tat | ggt | tcg | ggg | agt | tat | tat | acc | cac | ttt | gac | 336 |
| Ala | Lys | Gly | Phe | Gln | Tyr | Gly | Ser | Gly | Ser | Tyr | Tyr | Thr | His | Phe | Asp |     |

100 105 110  
 tac tgg ggc cag gga acc ctg gtc acc gtc tcc tca 372  
 Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
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 Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
 35 40 45  
 Ser Ala Ile Ser Gly Ser Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Glu  
 50 55 60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65 70 75 80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95  
 Ala Lys Gly Phe Gln Tyr Gly Ser Gly Ser Tyr Tyr Thr His Phe Asp  
 100 105 110  
 Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

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 Asp Ile Gln Met Thr Gln Ser Pro Ser Leu Ser Ala Ser Val Gly  
 1 5 10 15  
 gac aga gtc acc atc act tgt cgg gcg agt cag ggt att agc agc tgg 96  
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp  
 20 25 30  
 tta gcc tgg tat cag cag aaa cca gag aaa gcc cct aag tcc ctg atc 144  
 Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile  
 35 40 45

tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc 192  
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly  
           50                          55                          60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
           65                          70                          75                          80

gaa gat ttt gca act tat tac tgc caa cag tat aat agt tac ccg tac 288  
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr  
                                   85                          90                          95

act ttt ggc cag ggg acc aag ctg gag atc aaa 321  
 Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
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 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp  
                           20                          25                          30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile  
           35                          40                          45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly  
           50                          55                          60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
           65                          70                          75                          80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr  
                           85                          90                          95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
           100                          105

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 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg  
           1                          5                          10                          15

tcc ctg aga ctc tcc tgt gca gcg tct gga ttc acc ttc agt agc tat 96

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Thr | Phe | Ser | Ser | Tyr |     |  |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |     |  |
| gac | ata | cac | tgg | gtc | cgc | cag | gct | cca | ggc | aag | ggg | ctg | gag | tgg | gtg | 144 |  |
| Asp | Ile | His | Trp | Val | Arg | Gln | Ala | Pro | Gly | Lys | Gly | Leu | Glu | Trp | Val |     |  |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |  |
| gca | gta | ata | tgg | tat | gat | ggc | agt | aat | aaa | tac | cat | gca | gac | tcc | gtg | 192 |  |
| Ala | Val | Ile | Trp | Tyr | Asp | Gly | Ser | Asn | Lys | Tyr | His | Ala | Asp | Ser | Val |     |  |
|     |     | 50  |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |     |  |
| aag | ggc | cga | ttc | acc | atc | tcc | aga | gac | aat | tcc | aag | aac | acg | ctg | tat | 240 |  |
| Lys | Gly | Arg | Phe | Thr | Ile | Ser | Arg | Asp | Asn | Ser | Lys | Asn | Thr | Leu | Tyr |     |  |
|     | 65  |     |     |     | 70  |     |     |     | 75  |     |     |     |     | 80  |     |     |  |
| ctg | caa | atg | aac | agt | ctg | aga | gcc | gag | gac | acg | gct | gtg | tat | tac | tgt | 288 |  |
| Leu | Gln | Met | Asn | Ser | Leu | Arg | Ala | Glu | Asp | Thr | Ala | Val | Tyr | Tyr | Cys |     |  |
|     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |  |
| gcg | aga | aac | tat | ggg | ttg | ggg | agt | tat | tat | aac | tac | ttt | gac | ttc | tgg | 336 |  |
| Ala | Arg | Asn | Tyr | Gly | Leu | Gly | Ser | Tyr | Tyr | Asn | Tyr | Phe | Asp | Phe | Trp |     |  |
|     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |  |
| ggc | cag | gga | acc | ctg | gtc | acc | gtc | tcc | tca |     |     |     |     |     |     | 366 |  |
| Gly | Gln | Gly | Thr | Leu | Val | Thr | Val | Ser | Ser |     |     |     |     |     |     |     |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     |     |     |     |     |     |  |

&lt;210&gt; 6

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 6

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| Gln | Val | Gln | Leu | Val | Glu | Ser | Gly | Gly | Gly | Val | Val | Gln | Pro | Gly | Arg |  |  |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |  |  |
| Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Thr | Phe | Ser | Ser | Tyr |  |  |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |  |  |
| Asp | Ile | His | Trp | Val | Arg | Gln | Ala | Pro | Gly | Lys | Gly | Leu | Glu | Trp | Val |  |  |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |  |  |
| Ala | Val | Ile | Trp | Tyr | Asp | Gly | Ser | Asn | Lys | Tyr | His | Ala | Asp | Ser | Val |  |  |
|     |     | 50  |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |  |
| Lys | Gly | Arg | Phe | Thr | Ile | Ser | Arg | Asp | Asn | Ser | Lys | Asn | Thr | Leu | Tyr |  |  |
|     | 65  |     |     |     | 70  |     |     |     | 75  |     |     |     |     | 80  |     |  |  |
| Leu | Gln | Met | Asn | Ser | Leu | Arg | Ala | Glu | Asp | Thr | Ala | Val | Tyr | Tyr | Cys |  |  |
|     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |  |  |
| Ala | Arg | Asn | Tyr | Gly | Leu | Gly | Ser | Tyr | Tyr | Asn | Tyr | Phe | Asp | Phe | Trp |  |  |
|     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |  |  |
| Gly | Gln | Gly | Thr | Leu | Val | Thr | Val | Ser | Ser |     |     |     |     |     |     |  |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     |     |     |     |     |  |  |

&lt;210&gt; 7

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<220>  
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<400> 7

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
  1              5              10              15

gac aga gtc acc atc act tgt cgg gcg agt cat ggt att agc agc tgg      96
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser His Gly Ile Ser Ser Trp
              20              25              30

tta gcc tgg tat cag cag aaa cca gag aaa gcc cct aag tcc ctg atc     144
Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
              35              40              45

tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc     192
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
              50              55              60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct     240
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
              65              70              75              80

gaa gat ttt gca act tat tac tgc caa cag tat aat agt tac ccg tac     288
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
              85              90              95

act ttt ggc cag ggg acc aag ctg gag atc aaa                        321
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
              100              105

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<400> 8

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser His Gly Ile Ser Ser Trp
              20              25              30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
              35              40              45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
              50              55              60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
              65              70              75              80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr

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85

90

95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
 100 105

&lt;210&gt; 9

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1) .. (366)

&lt;400&gt; 9

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| cag | gtg | cag | ctg | gtg | gag | tct | ggg | gga | ggc | gtg | gtc | cag | cct | ggg | agg | 48  |
| Gln | Val | Gln | Leu | Val | Glu | Ser | Gly | Gly | Gly | Val | Val | Gln | Pro | Gly | Arg |     |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| tcc | ctg | aga | ctc | tcc | tgt | gca | gcg | tct | gga | ttc | acc | ttc | agt | agc | tat | 96  |
| Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Thr | Phe | Ser | Ser | Tyr |     |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| gtc | atg | cac | tgg | gtc | cgc | cag | gct | cca | ggc | aag | ggg | ctg | gag | tgg | gtg | 144 |
| Val | Met | His | Trp | Val | Arg | Gln | Ala | Pro | Gly | Lys | Gly | Leu | Glu | Trp | Val |     |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     |     | 45  |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| gca | gtt | ata | tgg | tat | gat | gga | agt | aat | aaa | tac | tat | gca | gac | tcc | gtg | 192 |
| Ala | Val | Ile | Trp | Tyr | Asp | Gly | Ser | Asn | Lys | Tyr | Tyr | Ala | Asp | Ser | Val |     |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| aag | ggc | cga | ttc | acc | atc | tcc | aga | gac | aat | tcc | aag | aac | acg | ctg | tat | 240 |
| Lys | Gly | Arg | Phe | Thr | Ile | Ser | Arg | Asp | Asn | Ser | Lys | Asn | Thr | Leu | Tyr |     |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| ctg | caa | atg | aac | agc | ctg | aga | gcc | gag | gac | acg | gct | gtg | tat | tac | tgt | 288 |
| Leu | Gln | Met | Asn | Ser | Leu | Arg | Ala | Glu | Asp | Thr | Ala | Val | Tyr | Tyr | Cys |     |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| gcg | ctt | atg | gtt | cgg | gga | ctt | att | ata | acg | ggg | tac | ttt | gac | tac | tgg | 336 |
| Ala | Leu | Met | Val | Arg | Gly | Leu | Ile | Ile | Thr | Gly | Tyr | Phe | Asp | Tyr | Trp |     |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| ggc | cag | gga | acc | ctg | gtc | acc | gtc | tcc | tca |     |     |     |     |     |     | 366 |
| Gly | Gln | Gly | Thr | Leu | Val | Thr | Val | Ser | Ser |     |     |     |     |     |     |     |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     |     |     |     |     |     |

&lt;210&gt; 10

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Gln | Val | Gln | Leu | Val | Glu | Ser | Gly | Gly | Gly | Val | Val | Gln | Pro | Gly | Arg |  |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |  |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
| Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Thr | Phe | Ser | Ser | Tyr |  |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |  |

Val Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val  
           50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
       65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95

Ala Leu Met Val Arg Gly Leu Ile Ile Thr Gly Tyr Phe Asp Tyr Trp  
                  100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
      115                 120

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 Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly  
      1                  5                  10                  15

gaa aga gcc acc ctc tcc tgc agg gcc agt cag agt gtt agc agc tac 96  
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr  
           20                  25                  30

tta gcc tgg tac caa cag aaa cct ggc cag gct ccc agg ctc ctc atc 144  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile  
           35                  40                  45

tat gat gca tcc aac agg gcc act ggc atc cca gcc agg ttc agt ggc 192  
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly  
           50                  55                  60

agt ggg tct ggg aca gac ttc act ctc acc atc agc agc cta gag cct 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro  
       65                  70                  75                  80

gaa gat ttt gca gtt tat tac tgt cag cag cgt agc aac tgg cct ccg 288  
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro  
           85                  90                  95

tac act ttt ggc cag ggg acc aag ctg gag atc aaa 324  
 Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
          100                 105

<210> 12  
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 <213> Homo sapiens

&lt;400&gt; 12

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly  
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr  
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile  
 35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly  
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro  
 65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro  
 85 90 95

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys  
 100 105

&lt;210&gt; 13

&lt;211&gt; 3159

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: cloning vector

&lt;400&gt; 13

aattagcggc cgctgtcgac aagcttcgaa ttcagtatcg atgtggggta cctactgtcc 60  
 cgggattgcg gatccgcgat gatatcggtg atcctcgagt gcggccgcag tatgcaaaaa 120  
 aaagcccgt cattagggcg gctcttggca gaacatatcc atcgcggtccg ccactctccag 180  
 cagccgcacg cggcgcatct cgggcagcgt tgggtcctgg ccacgggtgc gcatgatcgt 240  
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